ESTABLISHING HCG CUTOFFS AFTER FROZEN EMBRYO TRANSFER TO PREDICT IVF SUCCESS

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Introduction

Frozen embryo transfer (FET) is followed by close monitoring with quantitative HCG levels and ultrasounds to ensure a viable pregnancy. HCG is the first observable trophoblast proliferation signal in maternal blood after embryo implantation. Several studies have confirmed that serum HCG is a reliable indicator for predicting early pregnancy at 12–18 days post-transfer (1). Previous research has examined the predictive value of HCG levels on the seventh day after FET for ongoing pregnancy. An HCG cutoff level of 4.34 mIU/mL on day seven has demonstrated high predictive value for ongoing pregnancy (1). These studies focus on ongoing pregnancy as the critical endpoint for IVF. However, there is no established cutoff for HCG levels on day 14, nor is it clear whether this value can guide discontinuation of progesterone support, withdrawal of pregnancy attempts, or its correlation with the presence of fetal cardiac activity.

Often in FET cycles, an HCG level is drawn on day 14 to assess pregnancy viability. This level influences the decision to continue or discontinue progesterone supplementation. However, this determination is often based on clinical judgment, as there is no published literature establishing a definitive cutoff value. Following this, an ultrasound is typically performed five weeks post-FET.

A fetal heartbeat can be detected as early as 31 days (2). In cases where HCG levels are subjectively low but progesterone support is continued, there is often a three-week wait to confirm viability. However, if HCG is considered low and progesterone is discontinued, the pregnancy is lost. This period of uncertainty can be emotionally distressing for patients, and the lack of clear HCG thresholds does not provide confidence in clinical decision-making.

Objectives

1. Determine HCG level is the clinical cutoff to stop progesterone and deem the transfer unsuccessful.

2. Evaluate what 2-week post FET HCG level predicts the presence of a fetal heart beat at 5 weeks following embryo transfer.

The overall goal is to determine how the HCG and ultrasound findings impact the decision to continue or withdraw progesterone supplementation following FET.

Methods

This IRB-approved retrospective cohort study included natural and programmed FETs at a single fertility center from January to December 2023. First hCG levels were measured 14 days post-FET. Data collected from electronic medical records included demographics, embryo grading, preimplantation genetic testing, medications, progesterone type, estrogen levels, endometrial thickness, HCG levels at 14 days post-FET, (FHT) at 6 weeks, and (LB). Hc CG levels were stratified to determine predictive cutoffs for FHT and LB. The predictive model's performance was assessed using accuracy, sensitivity, specificity, and ROC AUC metrics.
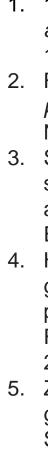
Results

Table 1: HCG levels associated with live birth

Live birth Row%

Factor	No (N=239)	Yes (N=321)
Post embryo transfer HCG at 14 days	0.00 [0.00, 32.6]	1532.0 [1036.0, 2175.0]
HCG by zero		
0	154 (100.0)	0 (0.00)
>0	85 (20.9)	321 (79.1)
HCG levels		
0	154 (100.0)	0 (0.00)
(0-100]	36 (100.0)	0 (0.00)
(100-200]	8 (88.9)	1 (11.1)
(200-300]	5 (45.5)	6 (54.5)
(300-400]	4 (44.4)	5 (55.6)
(400-500]	2 (22.2)	7 (77.8)
(500-600]	3 (25.0)	9 (75.0)
(600-1000]	9 (17.3)	43 (82.7)
(1000-2000]	13 (7.8)	154 (92.2)
2000+	5 (5.0)	96 (95.0)
HCG by 289 cut-off		
HCG < 289	203 (98.1)	4 (1.9)
HCG >= 289	36 (10.2)	317 (89.8)

Table 2: : HCG levels associated with fetal heart beat

Fetal heart Row%

Factor	No (N=222)	Yes (N=338)
Post embryo transfer hCG at 14 days	0.00 [0.00, 5.5]	1513.0 [1015.0, 2158.0]
HCG by zero		
0	149 (96.8)	5 (3.2)
>0	73 (18.0)	333 (82.0)
HCG levels		
0	149 (96.8)	5 (3.2)
(0-100]	35 (97.2)	1 (2.8)
(100-200]	7 (77.8)	2 (22.2)
(200-300]	5 (45.5)	6 (54.5)
(300-400]	3 (33.3)	6 (66.7)
(400-500]	2 (22.2)	7 (77.8)
(500-600]	3 (25.0)	9 (75.0)
(600-1000]	6 (11.5)	46 (88.5)
(1000-2000]	9 (5.4)	158 (94.6)
2000+	3 (3.0)	98 (97.0)
HCG by 289 cut-off		
HCG < 289	196 (94.7)	11 (5.3)
HCG >= 289	26 (7.4)	327 (92.6)

Statistics presented as Median [P25, P75], N (row %).

Results

Presence of Fetal Heart Tones and Live Birth Rate by hCG Cutoff

Fetal Heart Tones	No (N=222)	Yes (N=338)
HCG by 289 cut-off		
HCG < 289	196 (94.7)	11 (5.3)
HCG >= 289	26 (7.4)	327 (92.6)
Live Birth	No (N=239)	Yes (N=321)
hCG by 289 cut-off		
HCG < 289	203 (98.1)	4 (1.9)
HCG >= 289	36 (10.2)	317 (89.8)

Statistics presented as Median [P25, P75], N (row %).

Among the 560 FETs analyzed, 60.4% (n=338) resulted in FHT, and 57.3% (n=321) led to LB. The optimal hCG cutoff at 14 days post-FET for predicting LB was 289 mIU/mL (Table 1), with an accuracy of 92.9% (CI: 90.7–95.0), sensitivity of 98.8% (CI: 97.5–100), and specificity of 84.9% (CI: 90.4–89.5). Notably, the lowest hCG level associated with LB was 147 mIU/mL. The model achieved excellent ROC AUC values for predicting FHT (0.95) and LB (0.96).

Conclusion

This study provides valuable insights for managing early pregnancies after FET. An hCG level of 289 mIU/mL at 14 days post-FET has strong predictive value for FHT and LB, which has yet to be demonstrated in the literature. This study offers a critical threshold for counseling patients regarding decisions on continuing progesterone support after FET.

References

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